UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,412	01/22/2001	Ruowen Ge	1781-0215P	7335

2292 7590 10/16/2006

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 10/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/766,412	GE ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-8,10,13-16,19,20,25-27 and 29-32* is/are pending in the application.

4a) Of the above claim(s) *30-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-8,10,13-16,19,20 and 29* is/are rejected.

7)☐ Claim(s) *25-27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT TO AMENDMENT, REMARKS, STATUS OF THE APPLICATION AND CLAIMS

1. The amendment and remarks filed 08/23/06 are acknowledged, entered and considered. In view of Applicant's request claims 22, 23 and 28 have been canceled. Claims 1, 2, 6-8, 10, 13-16, 19, 20, 25-27 and 29-32 are now pending in the application of which claims 30-32 are withdrawn for election by original presentation for the reasons discussed in the previous Office action. Thus, the Office action is directed to the merits of claims 1, 2, 6-8, 10, 13-16, 19, 20, 25-27 and 29 as *per* elected invention. The rejection under 35 U.S.C. 112, first paragraph for claims 22, 23 and 28 is withdrawn in view of Applicant's cancellation of the claims. However, the rejection under 35 U.S.C. 112, first paragraph for claims 1, 2, 6-8, 10,13-16, 19, 20 and 29 are maintained for the reasons of record.

CLAIMS REJECTION-35 U.S.C. 112, 1st PARAGRAPH

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 6-8, 10, 13-16, 19, 20 and 29 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no description in the instant specification for the claimed peptide comprising a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide as claimed in independent claim 1.

Applicant's arguments filed 08/23/06 have been fully considered but they are not persuasive. Applicant has argued that it is not clear how the rejection stated by the Examiner on pages 5-10 of the Office Action applies to claims 10, 15, 16 and 20 is unpersuasive. Contrary to Applicant's arguments, claim 10 depends on claim 1and comprises a peptide having an amino acid sequence selected from the group consisting of SEQ ID NOS: 30-32, and claims 15, 16 and 20 depend on claim 10. Thus, the rejection clearly applies to claims 10, 15, 16 and 20 which depend directly or indirectly from claim 1.

Applicant further argued that endostatin is a well-known polypeptide of 184 amino acids. In addition to its biological recitation, claim 1 herein recites a peptide that comprises: a portion of an endostatin protein, wherein said peptide is of length from7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus peptide". There are only a finite number of 7-amino acid portions of the endostatin peptide, even fewer 8-amino acid portions, and fewer yet of the larger portions up to the 20-amino acid portions. A ***person skilled in the art***, upon reading the present specification, could readily envision

the list of all the recited 7-20 amino acid "portions" of endostatin. That list would, of course, contain far more peptides than are covered by claim 1. A ***person skilled in the art***, having read the specification, would learn what portion of the endostatin polypeptide should be obtained and would readily envision how to eliminate from the 'all 7-20 amino acid portions' list those portions that did not contain a pair of proline residues, at least one of which is at or penultimate to a terminus of the peptide "portion" of the 184 amino acid endostatin sequence. These two manipulations of the endostatin sequence, each of which is within the expected skill of the art, would leave the small group of proline-pair peptides that represent structures within claim 1. Applicant contends that there is nothing in the assay claimed (i.e., a bovine aorta endothelial cell proliferation assay) that is beyond the expected skill of those persons to whom the present disclosure is directed. The present disclosure provides ***persons skilled in the art*** with a written description of the claimed invention and concludes by stating the term "variant" does not appear in claim 1, it appears only in the Examiner's arguments is noted and is unpersuasive.

Contrary to Applicant's arguments, the claims as drafted read on peptides having length from 7-20 amino acids long (claim 1), length of 9 to 20 amino acids (claim 7), SEQ ID NOS: 30-32 (claim 10). Although, the term "variants" does not appear in claim 1, nevertheless, claims 1, 7 and 10 encompass all the fragments cited above. Further, the breadth of claim 1 is broad and encompasses unspecified fragments regarding the length from 7-20 amino acids long and containing a pair of proline residues penultimate to a terminus of the peptide. No reference sequence has been provided. There is no

written description indicating the claimed fragments for the peptide containing a pair of proline residues at least one of which is a terminal residue penultimate to a terminus of the peptide having 7-20 amino acid length except for the elected invention of the peptide having the amino acid sequences of SEQ ID NO:30. There are no written description for other peptides comprising a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide being made or used in the instant specification.

The use of 7-20 amino acid residues with any peptide comprising a portion of an endostatin protein suggests that the amino acid sequence/residue intended to be modified by substitution is either is not known or Applicant contemplates modification of a portion of an endostatin protein by substitution from 0 to 20 of amino acid residues in the peptide. Thus, the scope of the claims is not commensurate with the written description and/or enablement provided by the disclosure with regard to the amino acid residues identified by substitution of 7-20 amino acid residues with any portion of an endostatin protein for the reasons of record.

Furthermore, Applicant has provided a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide as disclosed in SEQ ID NO:30. From this Applicant is attempting to extrapolate to a broad diversity of a portion of an endostatin protein bearing little relationship to an endostatin comprising SEQ ID NO:30 disclosed in the

specification by claiming the substitution of any amino acid residue having less than 20 amino acids in length. For further support, see e.g., Figure 1B of Perletti et al, Cancer Research, Vol. 60, pages 1793-1796, April 1, 2001 (cited of PTO-892), which the amino acid sequence of the region containing rat endostatin is aligned with corresponding regions of murine and human sequences. Thus, in claim 1, any number of amino acids (at least from 0 to 20) can be replaced with any number ranging from 7-20 conservative or non-conservative amino acid residues. The effects of this are unknown for the reasons of record, and as such, when this fragment is added, the claimed invention becomes little more than conjecture. Moreover, without guidance and/or written description, the changes which can be made in the peptide/protein structure and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessary and improperly, extensive and undue. See Amgen Inc. V. Chuqai Pharmaceutical Co. Ltd., 927 F.2d, 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

Therefore, the scope of a peptide comprising a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide disclosed in the instant specification would involve substitution of the amino acid residues in the portion of an endostatin protein with any number of amino acid residues ranging from 7-20 conservative or non-conservative. Hence, it would include those that have not been shown or taught or described to be useful or enabled by the disclosed method of making ad using the invention. Moreover, undue

experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled, since any number of amino acid residues ranging from 7-20 are to be substituted with any amino acids identified as an endostatin protein are contemplated and are encompassed as well as wide range of situations. The results desired appear to be highly dependent on all fragments, the relationship of which is not clearly disclosed. Thus, without guidance and/or written description through working example(s), one of ordinary skill in the art would not predict from the sequence data disclosed in the instant specification to substitute any number of amino acid residues with a range of at least 7-20 amino acids and be used as a pharmaceutical formulation by administering a therapeutically effective amount of said pharmaceutical formulation to inhibit angiogenesis in tumor by administering the composition claimed to a subject in the manner claimed in the instant invention of claims 1, 2, 6-8, 10, 13-16, 19, 20 and 29.

Therefore, the specification does not disclose one reasonable method of making and using the claimed invention that bears a reasonable correlation to the entire scope of the claims. The specification lacks guidance/direction and/or written description as to how employ a peptide comprising a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide in the manner as claimed in the instant invention. In summary, the scope of the claims is broad, the written description does not demonstrate the claimed fragments of endostatin protein or peptide having 7-20 amino acid long, the effects of the claimed

peptide is unpredictable, and the teachings or the written descriptions in the specification are limited, therefore, it is necessary to have additional guidance and/or written description to carry out further experimentation to assess the effects of a peptide comprising a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide in the manner claimed in the instant invention of claims 1, 2, 6-8, 10, 13-16, 19, 20 and 29.

CITATION OF RELEVANT PRIOR ART

3. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Perletti et al (Cancer Research, Vol. 60. pp. 1793-1796, April 1, 2001) reports the cloning, expression, and antitumor activity of the rat form of endostatin.

OBJECTION TO CLAIMS, ALLOWABLE SUBJECT MATTER

4. Claims 25-27 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

ACTION IS FINAL

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CONCLUSION AND FUTURE CORRESPONDANCE

6. Claims 1, 2, 6-8, 10, 13-16, 19, 20 and 29 are rejected, claims 25-27 are objected and claims 30-32 are withdrawn as non-elected invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on (571) 272 0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JON WEBER
SUPERVISORY PATENT EXAMINER

Mohamed/AAM
October 10, 2006